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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,812	04/16/2004	Corey S. Goodman	18941H-002911US	1573

20350 7590 02/12/2007

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,812	GOODMAN ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-28* is/are pending in the application.

4a) Of the above claim(s) *20-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/16/4*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence alignment, one page*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I and species of a fragment 68-167 of SEQ ID NO: 8 in the reply filed on January 08, 2007 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden for the Examiner to examine Groups VII, IX and XI together with the elected Group I (p. 2 of the Response). This is not found persuasive because an application may properly be required to be restricted to one of two or more claimed inventions if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04 (j)) or distinct (MPEP § 806.05 - § 806.05 (i)). The Examiner has shown that the Groups I, VII, IX and XI are independent or distinct for the reasons in the previous Office action (see Paper mailed on November 02, 2006). Furthermore, MPEP § 803 provides that the separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a *prima facie* case that the search and examination of the plural inventions would impose a serious burden upon the Examiner; such separate classification was set forth in the Office action mailed on November 02, 2006.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 20-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on January 08, 2007.

3. Claims 10-19 are under examination in the instant office action.

Sequence compliance

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence identification has been provided for the nucleic and amino acid sequence presented on pages 11-12, 15-19, 28-29 and 33-34 of the instant specification. In case these sequences are new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

Claim Objections

5. Claim 17 is objected to because of the following informalities: the claim contains a period in the middle of the claim.

MPEP 608.01(m), Form of Claims, states:

Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, 36 USPQ2d 1211 (D.D.C. 1995).

Appropriate correction is required.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 10-19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility. The instant application has provided a description of an isolated protein and antibodies that bind to that protein. The instant application does not disclose a specific biological role for this protein and antibodies that bind to it or their significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess

anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to isolated antibodies that specifically bind to a protein of SEQ ID NO: 8. It is clear from the instant specification that the claimed novel antibodies bind to a human protein designated Robo 1, which shares sequence similarity with other proteins of Robo family, such as *Drosophila robo 2* and *C. elegans robo* (page 4 and Table 1 at pp. 5-8 of the instant specification). More specifically, "*robo* encodes a new class of guidance receptor with 5 Ig domains, 3 fibronectin (FN) type III domains, a transmembrane domain, and a long cytoplasmic domain. Robo defines a new subfamily of Ig superfamily proteins that is highly conserved from fruit flies to mammals. The results of protein expression and transgenic rescue experiments indicate that Robo functions as the gatekeeper controlling midline crossing and that Robo responds to an unknown midline repellent" (pages 2-3). Therefore, based on the structural similarities to different proteins with similar structural domains, it has been suggested that the human Robo 1 of SEQ ID NO: 8 of the instant invention would possess biological activity described as regulation of "cell, especially nerve cell, function and morphology" (p. 3).

Numerous publications exist on a topic of predicting protein functions from structural similarities or homology to the known proteins. It is well described in the art that amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36 and the whole paper). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification schemes) (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus, according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics. In the instant case, since specific biological functions of other moleculaes of class of Robo proteins at the time of invention appears to be unknown, no extrapolation of functional significance based on the structural similarities to Robo class of molecules can be made.

In the absence of knowledge of the biological significance of this specific protein, human Robo 1, there is no immediately obvious patentable use for the Robo 1 antibodies. According to the specification of the instant application "[t]he subject domains provide Robo domain specific activity or function, such as Robo-specific cell, especially neuron modulating or modulating inhibitory activity, Robo-ligand-binding or binding inhibitory activity" (page 12). The instant specification fails to provide any evidence that Robo domains are associated with any function or activity that would be directly or specifically related to a pathological or physiological process, which would support their practical utility. To employ the protein and the claimed antibody that binds to this protein in the future binding assays (p. 12 of the specification) is not a "real world"

because it would eventually relate to a protein for which no biological function is known. The instant application also fails to demonstrate use of the antibody as a marker for any disease or condition (which would be a real world use). To employ an antibody of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the antibody that binds naturally occurring human protein of SEQ ID NO: 8 in their currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 10-19 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. Claims 10-12, 14-15 and 18-19 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 10 encompasses antibodies that bind to polypeptides having at least 95% sequence identity with a particular disclosed sequence. Claims 11, 12, 14, 15, 18 and 19 are dependent claims. The claims do not require that the polypeptide possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims encompass a genus of polypeptides that is defined only by sequence identity. However, the instant specification fails to describe the entire genus of proteins, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 8. The claims are drawn to antibodies that bind to proteins having at least 95% sequence identity with a particular disclosed sequence. Thus, the claims are not limited to a protein with a specific amino acid sequence. The claims only require that the polypeptides recited in the claims share some degree of structural similarity to the isolated protein of SEQ ID NO: 8. The specification only describes a protein having the amino acid sequence of SEQ ID NO: 8 and fails to teach or describe any other protein which lacks the amino acid sequence of SEQ ID NO: 8 and has the activities possessed by the isolated human Robo 1 protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim

is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the encoded polypeptide has the disclosed activity. The specification does not provide a complete structure of those polypeptides having at least 95% sequence identity with a polypeptide of SEQ ID NO: 8 and fails to provide a representative number of species for the encompassed genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the encompassed genus of polypeptides and, consequently, the claimed genus of antibodies.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated antibodies that bind to the full length of the polypeptide of SEQ ID NO: 8 meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 10-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 10 and 18 are vague and indefinite in so far as it employs the term "Robo" as a limitation. This term is appears to be novel, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of "Robo-specific" or "Robo-mediated signaling". Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of the term "Robo", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

14. Claims 11-17 and 19 are indefinite for being dependent from the indefinite claim.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 10-19 are rejected under 35 U.S.C. 102(e) as being anticipated by McCarthy et al., Pub. No.: US 2002/0150988 A1, 10/17/2002, filing date 04/18/1997.

Claims 10-19 encompass isolated antibodies that bind to a polypeptide of SEQ ID NO: 8. McCarthy et al. document discloses a polypeptide with 100% identity to the instant polypeptide 68-167 of SEQ ID NO: 8, see copy of the sequence alignment attached t the instant office action. The McCarthy et al. document further discloses antibodies that bind to the polypeptide 68-167 of SEQ ID NO: 8, [0021], [0129] - [0135] thus, fully anticipating the instant invention.

Double Patenting

17. Applicant is advised that should claim 14 be found allowable, claim 15 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case,

claim 14 is limited to the polypeptide of SEQ ID NO: 8, therefore, the scope of claims 14 and 15 appears to be the same.

Conclusion

18. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1649

February 6, 2007

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<!--StartFragment-->
RESULT 1
US-10-105-934-5
; Sequence 5, Application US/10105934
; Publication No. US20020150988A1
;   GENERAL INFORMATION:
;        APPLICANT: McCarthy, Sean A.
;                   Holtzman, Douglas
;        TITLE OF INVENTION: NOVEL MOLECULES OF THE FTHMA-070-
;                            RELATED PROTEIN FAMILY AND THE T85-RELATED PROTEIN
;                            FAMILY AND USES THEREOF
;        NUMBER OF SEQUENCES: 18
;        CORRESPONDENCE ADDRESS:
;             ADDRESSEE: Fish & Richardson P.C.
;             STREET: 225 Franklin Street
;             CITY: Boston
;             STATE: MA
;             COUNTRY: USA
;             ZIP: 02110-2804
;        COMPUTER READABLE FORM:
;             MEDIUM TYPE: Diskette
;             COMPUTER: IBM Compatible
;             OPERATING SYSTEM: DOS
;             SOFTWARE: FastSEQ for Windows Version 2.0
;        CURRENT APPLICATION DATA:
;             APPLICATION NUMBER: US/10/105,934
;             FILING DATE: 25-Mar-2002
;        PRIOR APPLICATION DATA:
;             APPLICATION NUMBER: US/09/062,389
;             FILING DATE: 17-APR-1998
;             APPLICATION NUMBER: 60/062,017
;             FILING DATE: 10-OCT-1997
;             APPLICATION NUMBER: 60/044,746
;             FILING DATE: 18-APR-1997
;        ATTORNEY/AGENT INFORMATION:
;             NAME: Meiklejohn, Anita L.
;             REGISTRATION NUMBER: 35,283
;             REFERENCE/DOCKET NUMBER: 09404/051001
;        TELECOMMUNICATION INFORMATION:
;             TELEPHONE: 617/542-5070
;             TELEFAX: 617/542-8906
;             TELEX: 200154
;   INFORMATION FOR SEQ ID NO: 5:
;        SEQUENCE CHARACTERISTICS:
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;             TYPE: amino acid
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;        FRAGMENT TYPE: internal
;        SEQUENCE DESCRIPTION: SEQ ID NO: 5:
US-10-105-934-5

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